

REMARKS

Claims 39-43, 70 and 80-86 are in the case.

The claims have been amended to more clearly define Applicants' invention.

No new matter has been added.

Applicants gratefully acknowledge acceptance of the Applicants' Request for Continuing prosecution under 37 CFR §1.114 and entry of amendments to Claims 82, 84 and 86, submitted on November 20, 2003. Applicants also acknowledge the removal of the rejection to Claims 82, 84 and 86 under 35 USC §112, 1st paragraph.

All claims stand rejected variously under 35 USC §112 and §103.

Paragraph numbers used below correspond to those of the pending Office Action.

Claim Objections

4. Claims 41, 82, 84 and 86 are objected to because of the following minor informalities:

- a) Claim 41 was missing a period punctuation mark at the end of the sentence; and
- b) Claims 82, 84 and 86 each had a semi-colon following "group consisting of" instead of a colon in part 1) c) (iv).

The claims have been amended to overcome these objections.

Claim Rejections – 35 USC § 112

5. Claims 82, 84, 86 and 43 are rejected under 35 USC §112, second paragraph for indefiniteness. Specifically, the Examiner argues that two different limitations are specified for the P2 promoter, wherein in step c)(iv) P2 is defined as a second floral specific promoter and in the last step of the methods, P2 is activated in the common germline.

Claims 82, 84 and 86 have been amended for clarity. In light of these claim amendments, the Applicants respectfully request removal of these rejections.

6. Claims 39-43, 70, and 80-86 stand rejected under 35 USC §112, first paragraph for lack of enablement. Specifically, the Examiner argues that the specification fails to teach that multiple SSR systems can be used together in the same plant and that the specification does not contain working examples that demonstrate the claimed methods. Applicants respectfully traverse.

As the examiner is well aware the test for whether a claim is enabled or not "...requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the

pertinent art to make and use the claimed invention.” [MPEP 2164.01]. In order to meet this test the skilled person should not be required to engage in undue experimentation. [*Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916)]. Guidance in determining whether undue experimentation is required is found in the factors enumerated by the Federal Circuit in *In re Wands* and include:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Applicants submit that the specification enables the person of skill in the art to make and use the present invention comprising the use of multiple SSR systems in a single plant without undue experimentation. The claims under consideration are not overly broad being limited to specific constructs activated in plants in specific sequence. The prior art did not teach the use of multiple SSR at the time the invention was made, however did teach the use of single SSR species in plants.. The level of the one of ordinary skill in this art is high and one of skill would be expected to be able to make and use the present invention comprising multiple SSR systems given the amount of direction provided by the inventor in the specification (see for example figures 3-8 and the accompanying discussion on pages 35-41 of the specification) in combination with what was known in the art. The presence of a working example is not determinative of whether undue experimentation is required, see MPEP 2164.02, where it is stated” [T]he specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.”

In support of the notion that undue experimentation is not required to enable the present claims it should be noted that following Applicants' constructive reduction to practice of the invention on November 17, 2000, several references demonstrate that multiple systems can be used in plants together. See, for example:

- U.S. 6,262,341 ("Method for the integration of foreign DNA into eukaryotic genomes", Issued 20010717) and U.S. 6,541,231 ("Method for the integration of foreign DNA into eukaryotic genomes", Issued 20030401), wherein a chimeric recombinase having Cre and Frt activity is shown to function effectively, when transformed into plant cells having an expression cassette encoding GUS driven by the ubiquitin promoter, wherein a sequence flanked by either identical FRT or loxP sites interrupted the GUS ORF. Specifically, the "Cre-FLPm chimeric recombinase is functional independently at either the FRT site or the loxP site, as measured by the ability to activate GUS activity following excision of sequences between two identical target sites, thereby bringing GUS activity under the control of the ubiquitin promoter." (Example 2 of U.S. 6,262,341).
- U.S. 6,455,315 ("Compositions and methods to stack multiple nucleotide sequences of interest in the genome of a plant", Issued 20020924), wherein the claims are drawn to a "method to combine multiple transfer cassettes at one location in a genome of a plant cell" using a first recombinase and a second recombinase, and wherein the first and second recombinase are not the same.

in view of the above Applicant submits that the use of multiple SSR systems in plants is enabled and would not require undue experimentation on the part of the skilled person to practice the invention.

In view of the above arguments Applicants respectfully request that the lack of enablement rejection made under 35 USC § 112 be removed and the claims reconsidered.

Claim Rejections – 35 USC § 103

7. Pending Claims 39-41, 43, 70, 80, 83 and 85 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Odell et al. "A" (*Mol. Gen. Genet.* 223: 369-378 (1990)), in combination with Lloyd et al. (*Mol. Gen. Genet.* 242: 653-657 (1994)), Applicants' admitted state of the prior art, and Odell et al. "B" (Use of Site-Specific Recombination Systems in Plants, in Homologous Recombination and Gene Silencing in Plants; Paszkowski, J., Ed.; Kluwer: Dordrecht, Germany, 1994; pp 219-270). The Examiner maintains that the cited references demonstrate that more than one site-specific recombinase system is active in plants, that the ability of site-specific recombinases to locate their target sites on individual chromosomes is quite impressive, and that one of ordinary skill in the art had a reasonable expectation of success that two different site-specific recombination systems can work in the same

plant without interfering with each other. Applicants again respectfully traverse the rejection and submit that this combination of references in no way teaches or suggests Applicants' invention, and therefore, fails to establish a *prima facie* case of obviousness.

The teachings of the cited art have been given previously. The arguments made by Applicants previously in response to this rejection are relevant and are incorporated herein by reference.

The Examiner relies on the teaching of Odell et al B in particular to suggest that the person of skill in the art would find the use of multiple SSR in plants would be obvious. Some of the key teachings of Odell et al B are abstracted below:

- Odell et al. "B" (*supra*): Odell et al. B teach uses of various site-specific recombination systems individually in plants. It is asserted that the versatility and high recombination frequency of these systems allow their use as tools for a wide range of studies and applications; specifically, the following applications are discussed:
 - (a) Control of gene expression by gene inactivation, wherein the authors propose that: *"This procedure could be valuable in particular plant species where multiple efficient selection markers are not available."* (page 260, last paragraph).
 - (b) Control of gene expression by gene activation, wherein the authors suggest that site specific recombination systems provide advantages over use of tissue-specific promoters when transgene expression may be detrimental to cell function and when it is desirable to produce chimeric tissues.
 - (c) Developmental analysis, wherein it is suggest that *"...different proportions of recombined cells in a tissue or a plant could be achieved by using promoters with varying activities to express the recombinase."* (page 262, first paragraph).
 - (d) Introduction & Expression of the recombinase, wherein the authors state that: *"If constitutive expression is not desired, the recombinase might also be activated at the appropriate time by regulating it with an inducible or tissue-specific promoter."* (page 262, last paragraph).
 - (e) Site-directed Integration, wherein the authors suggest that: *"...establishing an effective site-directed integration system for plants may be difficult.... Transient recombinase activity may be achieved by introducing mRNA or protein directly into cells."* (page 263, second paragraph).

(f) Chromosomal Engineering, wherein the authors discuss uses of site specific recombinases in conjunction with transposases.

No other suggestions are made concerning the applications for which site-specific recombination systems could be applied, and no teaching is provided to instruct the person of skill in the art to use multiple SSR systems in a single plant.

Applicants acknowledge the Examiner's observation that Odell et al B remarks on the specificity of various SSR systems (page 260), however fail to understand why that observation would suggest to the skilled person that multiple SSR systems would be functional in a single plant. Additionally, one of the salient features of the Applicants' invention as now claimed is that the second recombinase is actually activated at the appropriate time by indirectly regulating it with a first recombinase. Clearly, this concept is not suggested or anticipated by Odell et al. B, or another other teaching.

In support of Applicants' position that the person of skill in the art would not have found the use of multiple SSR systems obvious at the time the invention was made, Applicant's submit herewith a declaration made under Rule 132 from the principal author of Odell et al B declaring that, in her opinion, the present invention could not have been derived from the state of the art at the time the invention was made.

In light of the amendments to the Claims and technical arguments presented herein, the Applicants respectfully request the Examiner to withdraw the present objection and rejections, and to reconsider the claims as amended. It is believed a complete response has been made to the Official Action dated February 17, 2004, and that the application stands in condition for allowance. Such action is respectfully solicited.

Respectfully submitted,



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